UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/681,490	10/07/2003	Gilbert Thill	G-099US03DIV	7137

23557 7590 09/15/2006

SALIWANCHIK LLOYD & SALIWANCHIK
A PROFESSIONAL ASSOCIATION
PO BOX 142950
GAINESVILLE, FL 32614-2950

EXAMINER
SWITZER, JULIET CAROLINE

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 09/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

Office Action Summary	**Application No.** 10/681,490	**Applicant(s)** THILL, GILBERT	
	Examiner Juliet C. Switzer	**Art Unit** 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *30 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12 and 14-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 14-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.

4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ .

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: _____.

DETAILED ACTION

1. This action is written in response to applicant's correspondence received 6/30/06. Claims 1, 2, and 11 have been amended and claim 13 has been canceled. Claims 1-12 and 14-23 are pending. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. All new rejections in this office action are necessitated by applicant's amendments to the claims. **This action is FINAL.**

Claim Rejections - 35 USC § 103

2. Claims 1-12 and 14-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al. (US 5376526) in view of Wickermasinghe et al. (Biochimica et Biophysica Acta, 607 (1980) 411-419).

Brown et al teach a method which comprises the selection or isolation of heteroduplexes containing at least on internal single stranded region with a single stranded trap that involves the use of a recognition element that is benzoylated-naphthoylated-DEAE-cellulose (BNDC). Namely, Brown et al. teach the isolation of partially single stranded DNA from fully duplex DNA by using BNDC (see for example, Col. 7, lines 10-15; Col. 12, line 65-Col. 13, line 9). Brown et al. teach that under some circumstances it is desirable to isolate and map regions of the genome that represent differences between samples (Col. 3, 1st ¶; Col. 9, lines 9-25), and Brown et al. teach that genetic regions isolated by their methods may be cloned and analyzed for use in future diagnostic methods (Col. 8, lines 62-68). In the methods taught by Brown et al., heteroduplexes are formed between related DNA molecules (Col. 11, line 50- Col. 12, line 28), and the internal single stranded regions represent nucleotide differences between the two samples (Col. 6, line 67-Col. 7, line 9).

Regarding claim 2, Brown et al. teach a method which includes the steps of (a) obtaining a DNA sample containing related DNA molecules (Col. 3, lines 15-65); (b) denaturing the molecules (Col. 4, line 56); (c) annealing the denatured molecules to allow the formation of heteroduplexes (Col. 4, line 57; Col. 6, line 67-Col. 7, line 9); and (d) isolating or selecting the heteroduplex containing at least on single stranded region using a single-stranded trap comprising a recognition element that is BNDC (see for example, Col. 7, lines 10-15; Col. 12, line 65-Col. 13, line 9).

Regarding claim 3, the Brown et al. teaches reducing the size of the DNA molecules (Col. 4, lines 15-40; Col. 9, lines 25-35; Col. 11, lines 35-40).

Regarding claim 4, Brown et al. teach removing single stranded unannealed DNA (Col. 5, lines 15-18; Col. 12, lines 34-44), and teach ligating adaptors to flush ended heterohybrids (Col. 5, lines 47-51).

Regarding claims 6-9 and 15-18, Brown et al. teach that the nucleic acid samples can be from a single individual (i.e. single source, Col. 3), from different individuals (i.e. at least two different sources, Col. 3, lines 62-68), that the source will be genomic DNA, which inherently "comprises" cDNA fragments. Regarding claims 9 and 18, any genome has a "limited set of genes" since the total number of genes, even in a very large genome has a "limited" number of genes (as opposed to an infinite number of genes).

Regarding claim 10, Brown et al. teach mixing the sample with BNDC to the binding of the partially single stranded molecules (i.e. those molecules having internal single stranded regions) with the BNDC, formation of complexes and separation of the complexes by centrifugation or other means (Col. 7, lines 10-19; Col. 12, line 65-Col. 13, line 9).

Regarding claims 14 and 19, the differences in the complex genomic hybridizations taught by Brown et al. would inherently comprise insertions and deletions or one or more nucleotides. The claim recites that the replacement must be of at least 15 nucleotides but does not place a length limitation on the insertions or deletions.

Brown et al. do not teach a method wherein heteroduplexes are eluted from the single stranded trap. Brown et al. do not specifically teach, however, a method in which the molecules having single stranded regions are isolated on the BNDC are recovered and used in further analysis.

Wickermasinghe et al. teach that affinity chromatography on BNDC permits fractionation of fully double-stranded DNA from partially single-stranded DNA and exemplify methods wherein partially single-stranded DNA is eluted from a BNDC column separately from double-stranded DNA (p. 412, 1st full ¶ and p. 413, lines 2-3). Further regarding claim 11, Wickermasinghe et al. teach preparing a column with BNDC, washing the column with a buffer (i.e. equilibrating the column in a buffer), bring the column into contact with the sample to allow binding of molecules with single stranded regions and formation of complexes between the heteroduplexed molecules and the BNDC, and eluting DNA from the column (p. 412-413, heading "*Affinity chromatography on benzyolated naphthoylated DEAE-cellulose*"). During the elution of DNA from the column, DNA which are not bound to the column under elution conditions are removed from the column. Regarding claim 12, Wickermasinghe et al. teach washing the column with a buffers comprising 1M NaCl (p. 413). Regarding claim 21, the elution results in recovering the DNA from the complexes (p. 413).

Thus, at the time the invention was made, it would have been prima facie obvious to one of ordinary skill in the art to have modified the methods taught by Brown et al. so as to have separately eluted the nucleic acids containing single stranded regions from the BNDC columns used by Brown et al., using methods as demonstrated by Wickermasinghe et al. One would have been motivated to isolate the heteroduplexed molecules by the express teaching of Brown et al. that the BNDC column separates partially single stranded molecules from fully duplexed DNA (Col. 7, lines 10-13) and that an embodiment of genetic mapping looks to differences within genomes (Col. 3, 1st ¶; Col. 9, lines 9-25). Further, one would have been motivated to use a method wherein the heteroduplexes are eluted from the BNDC column by the success of Wickermasinghe et al. at using this method for the elution of such molecules, and in order to obtain the molecules which are bound to the BNDC in the methods taught by Brown et al. (see Col. 7, lines 10-19).

Brown et al. in view of Wickermasinghe et al. do not exemplify methods wherein the heteroduplexes are amplified, cloned or sequenced. However, given the express teachings of Brown et al. that under some circumstances it is desirable to isolate regions with nucleotide differences for further study, and the express suggestion by Brown et al. that sequences isolated should be cloned for further study, it would have been prima facie obvious to one of ordinary skill in the art to have modified the methods of Brown et al. so as to have recovered and cloned the nucleic acids with single stranded regions taught by Brown et al. One would have been motivated to recover these nucleic acids for the purpose of further study of genomic regions with nucleic acid differences. Brown et al. do not teach the steps of amplifying DNA with differences, repeating the isolation of molecules with single stranded regions, or of sequencing the DNA harboring differences. However, at the time the invention was made, each of these methodologies was routinely practiced in the prior art for the isolation, cloning, and study of nucleic acid sequences of interest. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the methods taught by Brown et al. to include any of these steps for the enrichment of the nucleic acids having single stranded regions that represented sequence differences taught by Brown et al. Thus, in light of the disclosure of Brown et al., the claimed invention is prima facie obvious.

Response to Remarks

The previously set forth 102 rejections and 103 rejection are overcome by applicant's amendments to the claims. New grounds of rejection are set forth in this office action to address the amendment of the claims. Applicant's remarks are against the previously set forth rejections and are moot in view of the new grounds of rejection. It is noted that Brown et al. do not exemplify the recovery of mismatched regions from the BNDC, however, as noted in the rejection Brown et al. expressly teach that sometimes the isolation of these molecules is desirable. The deficiencies in Brown et al. are met by the secondary rejection provided in this office action. Regarding the 103 rejection in view of Brown et al., applicant states that the purpose of the method used in Brown et al. is to identify regions which are mismatch-free heteroduplexes, citing the summary of the invention at column 2 of Brown et al. However, the very next paragraph of Brown et al., also in the summary of the invention teaches that one may also map regions of difference (See Col. 3), and in later portions of their description Brown et al.

teach state specifically "An alternate embodiment of genetic mapping looks to differences... (Col. 9, line 9)." One must consider a reference for all that it teaches. Applicant is reminded that MPEP 2123 teaches that "A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments."

Conclusion

3. No claim is allowed.

4. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C Switzer whose telephone number is (571) 272-0753. The examiner can normally be reached on Monday, Tuesday, or Thursday, from 9:00 AM until 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached by calling (571) 272-0735.

The fax phone numbers for the organization where this application or proceeding is assigned are (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-0507. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Juliet C. Switzer
Primary Examiner
Art Unit 1634

September 12, 2006